AMENDMENTS TO THE CLAIMS:

Please amend Claims 1 – 38 as follows:

1. (Currently Amended) A process for the ~~manufacturing~~ manufacture of NO-donating compounds comprising;~~step 1~~ (1),

$ML_{T1}A_{T2}$-COOH + HO-X-OH→ $ML_{T1}A_{T2}$-COO-X-OH

(I) (II)

using an acidic or dehydrating agent and a first solvent, optionally followed by purification using extraction or ~~crystallisation~~ crystallization, and

~~step 2~~ (2), $ML_{T1}A_{T2}$-COO-X-OH + RSO_2Cl → $ML_{T1}A_{T2}$-COO-X-OSO_2R,

(II) (III)

using a second solvent, a base and optionally a catalyst, followed by purification using extraction and ~~crystallisation~~ crystallization, and

~~step 3~~ (3),

$ML_{T1}A_{T2}$-COO-X-OSO_2R + Y-NO_m → $ML_{T1}A_{T2}$-COO-X-ONO_m

(III) (IV)

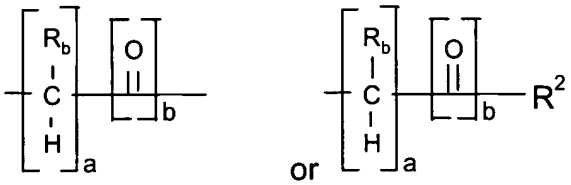
using a third solvent and optionally a catalyst,

optionally followed by a ~~crystallisation~~ crystallization process for obtaining the compound of formula IV in a substantially crystalline form, and

wherein:

M is a radical of a physiologically active compound;

L is O, S, (CO)O, (CO)NH, (CO)NR^1, NH, NR^1, wherein R^1 is a linear or branched alkyl group, or



wherein R_b is H, $C_{1\text{-}12}$ alkyl or $C_{2\text{-}12}$ alkenyl;

R^2 is (CO)NH, (CO)NR^1, (CO)O, or CR^1 and a and b are independently 0 or 1;

A is a substituted or unsubstituted straight or branched alkyl chain;

X is a carbon linker;

R is selected from the group consisting of C_1-C_8 alkyl, phenyl, phenylmethyl, C_1-C_4 alkylphenyl, halophenyl, nitrophenyl, acetylaminophenyl, halogen, CF_3 and *n*-C_4F_9;

Y-NO_3 is selected from the group consisting of lithium nitrate, sodium nitrate, potassium nitrate, magnesium nitrate, calcium nitrate, iron nitrate, zinc nitrate ~~or~~ and tetraalkylammonium nitrate, [[(]]wherein alkyl is a straight or branched C_1-C_{18}-alkyl~~, which may be straight or branched~~);

m is 1 or 2; and

T1 and T2 are each independently 0, 1, 2 or 3;

with the proviso that

when $ML_{T1}A_{T2}$-COOH is naproxen, then X is not $(CH_2)_4$.

2. (Currently Amended) The process according to claim 1, wherein group M is part of a molecule of an NSAID, COX 1 or COX 2 inhibitor.

3. (Currently Amended) The process according to claim 1, wherein X is selected from the group consisting of

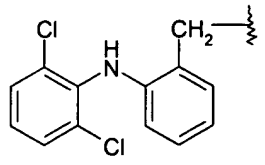
linear -$(CH_2)_{w1}$-, wherein w1 is an integer of from 2 to 6; -$(CH_2)_2$-O-$(CH_2)_2$-, and

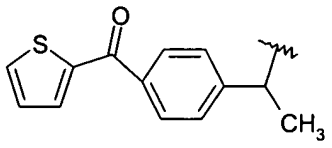
-CH_2-C_6H_4-CH_2-.

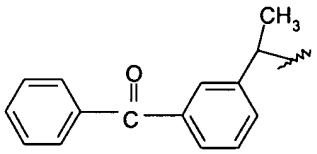
4. (Currently Amended) The process according to claim 1, wherein R is selected from the group consisting of

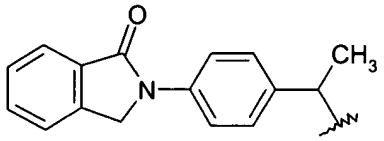
C_1-C_8-alkyl, phenyl, phenylmethyl, C_1-C_4-alkylphenyl, halophenyl, nitrophenyl, acetylaminophenyl, and halogen.

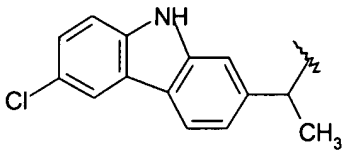
5. (Currently Amended) The process according to claim 1, wherein the group $ML_{T1}A_{T2}$ is selected from the group consisting of:

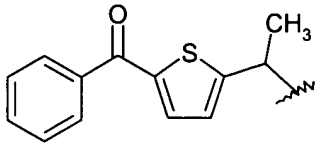


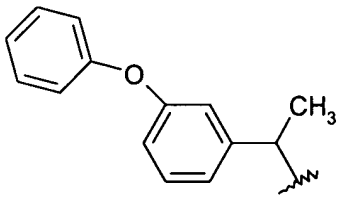


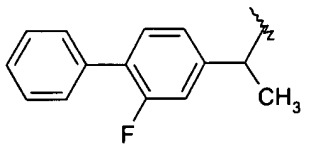


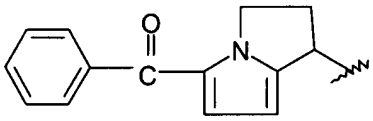


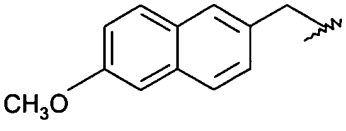


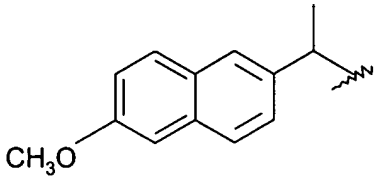


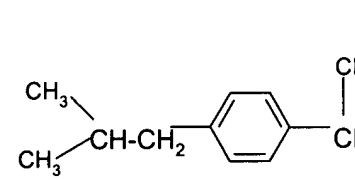


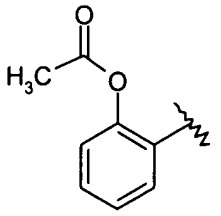




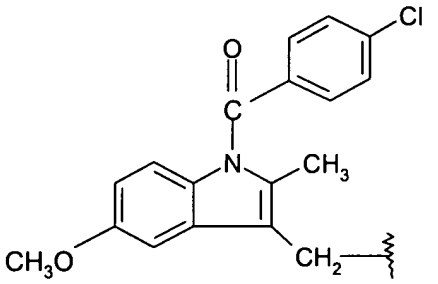




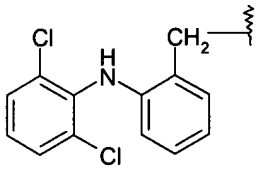




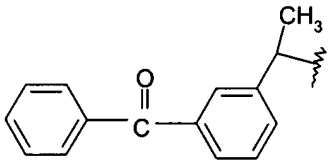
, and



6. (Currently Amended) The process according to claim 5, wherein the group $ML_{T1}A_{T2}$ is:



or



7. (Currently Amended) The process according to ~~any one of claims 1 to 6~~ claim 1, ~~whereby~~ wherein the ~~crystallisation~~ crystallization process for the compound of formula IV comprises ~~the following steps~~:

a) i) dissolving the compound in a fourth solvent;

or,

ii) extracting the compound from the reaction solution into a fourth solvent;

or,

iii) starting from the reaction solution comprising ~~said~~ the compound;

b) ~~vaporating~~ evaporating the fourth solvent;

c) adding an anti-solvent and/or cooling

d) isolating the crystals formed, and optionally;

e) ~~recrystallising~~ recrystallizing the crystals formed ~~in step c);~~ or isolated ~~in step d)~~.

8. (Currently Amended) The process according to claim 7, ~~whereby~~ wherein the ~~crystallisation~~ crystallization process for compound 2-[2-(nitrooxy)-ethoxy]ethyl{2-[(2,6-dichlorophenyl)amino]phenyl}acetate (IVa) comprises ~~the following steps~~:

a) extracting the compound from the reaction solution into ~~a~~ the fourth solvent;

b) evaporating the fourth solvent;

c) adding an anti-solvent and/or cooling;

d) isolating the crystals formed, and optionally;

e) ~~recrystallising~~ recrystallizing the crystals formed ~~in step c);~~ or isolated ~~in step d)~~.

9. (Currently Amended) The process according to ~~any one of claims 1 to 8~~ claim 1, ~~whereby an~~ wherein the acidic or dehydrating agent ~~in step 1~~ is selected from the group consisting of sulphuric acid or its salts, perchloric acid ~~(e.g. 70%) or other suitable acids such as~~ polystyrene sulphonic acids, zeolites, acidic clays, sand in combination with strong hydrophilic acids, ~~such as perchloric acid or gaseous hydrogen chloride~~ and montmorillonites.

10. (Currently Amended) The process according to ~~any one of claims 1 to 8~~ claim 1, ~~whereby~~ wherein the first solvent ~~in step 1~~ is a non-polar and/or non acidic solvent.

11. (Currently Amended) The process according to ~~any one of claims 1 to 10~~ claim 1, ~~whereby~~ wherein the second solvent is ~~solvents in step 2 are~~ selected from a group consisting of toluene, cumene, xylenes, ethyl acetate, acetonitrile, butyl acetate, and isopropyl acetate.

12. (Currently Amended) The process according to ~~any one of claims 1 to 10~~ claim 1, ~~whereby~~ wherein the base ~~in step 2~~ is triethylamine or *N*-methylmorpholine.

13. (Currently Amended) The process according to ~~any one of claims 1 to 10~~ claim 1, ~~whereby~~ wherein the catalyst ~~in step 2~~ is 4-(dimethylamino)pyridine.

14. (Currently Amended) The process according ~~to any one of claims 1 to 13~~ claim 1, ~~whereby~~ wherein the compound of formula III ~~in step 2~~ is ~~crystallised~~ crystallized from an organic solvent.

15. (Currently Amended) The process according to claim 14, ~~whereby~~ wherein an ~~antisolvent~~ anti-solvent is used in the crystallization of compound of formula III ~~in step 2.~~

16. (Currently Amended) The process according to ~~any one of claims 1 to 15~~ claim 1, ~~whereby the nitrate sources~~ wherein Y-NO_3 ~~in step 3~~ is selected from the group consisting of lithium nitrate, sodium nitrate, potassium nitrate, magnesium nitrate, ~~and~~ calcium nitrate, ~~or~~ and mixtures thereof.

17. (Currently Amended) The process according to ~~any one of claims 1 to 15~~ claim 1, ~~whereby~~ wherein the third organic solvent ~~in step 3~~ is selected from the group consisting of *N*-methylpyrrolidinone, sulpholane, tetramethylurea, 1,3-dimethyl-2-imidazolidinone, acetonitrile, methyl isobutylketone, ethyl acetate, butyl acetate, ~~and~~ isopropyl acetate, ~~or~~ and mixtures thereof.

18. (Currently Amended) The process according to ~~any one of claims 1 to 15~~ claim 1, ~~whereby~~ wherein the phase transfer-catalyst ~~in step 3~~ is selected from the group consisting of tetraalkylammonium salt, arylalkylammonium salt, tetraalkylphosphonium salt, arylalkylphosphonium salt, crown ether, pentaethylene glycol, hexaethylene glycol, ~~and~~ polyethylene glycols, ~~or~~ and mixtures thereof.

19. (Currently Amended) The process according to ~~any one of claims 7 or 8~~ claim 7, ~~whereby~~ wherein the fourth solvent ~~in step a)~~ is selected from the group ~~comprising~~ consisting of lower alkyl acetates, lower alkyl alcohols, aliphatic hydrocarbons, aromatic hydrocarbons, heteroaromatic hydrocarbons, dialkyl ketones, dialkyl ethers, nitriles, ~~and~~ water, ~~or~~ and mixtures thereof.

20. (Currently Amended) The process according to ~~any one of claims 7 or 8~~ claim 7, ~~whereby~~ wherein the anti-solvent ~~the antisolvent in step b) of the crystallisation process~~ is selected from the group ~~comprising~~ consisting of ethanol, ~~or~~ 2-propanol,

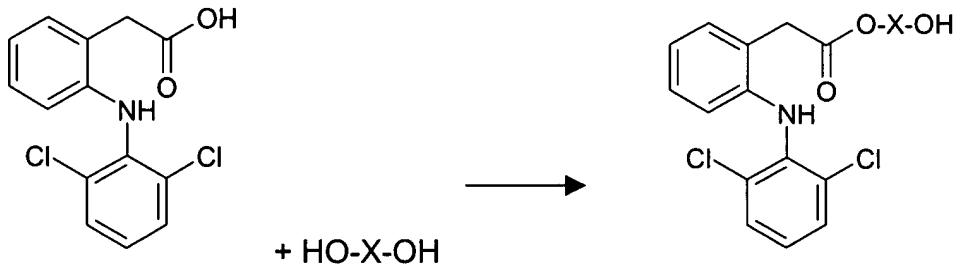
toluene, cumene, xylenes, ligroin, petroleum ether, halobenzenes, heptanes, hexanes, octanes, cyclohexanes, ~~and~~ cycloheptanes, ~~or~~ and mixtures thereof.

21. (Currently Amended) The process according to ~~any one of claims 7 or 8~~ claim 7, ~~whereby~~ wherein the solvent in step d) is selected from the group consisting of toluene, cumene, xylenes, methyl *iso*-butyl ketone, di-*n*-butyl ether, *tert*-butyl methyl ether, tetrahydrofuran, acetonitrile, *n*-butyl acetate, ~~and~~ dichloromethane, ~~or~~ and mixtures thereof.

22. (Currently Amended) The process according to ~~any one of claims 1 to 21~~ claim 1, ~~whereby~~ wherein the process is conducted at a temperature ~~is~~ between -40°C and 120°C.

23. (Currently Amended) A process for the ~~manufacturing~~ manufacture of NO donating diclofenac of formula IVa, IVb or IVc, comprising:

~~step 1~~ (1), reacting a compound of formula Ia with HO-X-OH, wherein X is $C_2H_4OC_2H_4$, C_4H_8, or $C_2H_4OC_2H_4OC_2H_4$, to obtain compounds of formula IIa, IIb or IIc,



diclofenac (Ia)

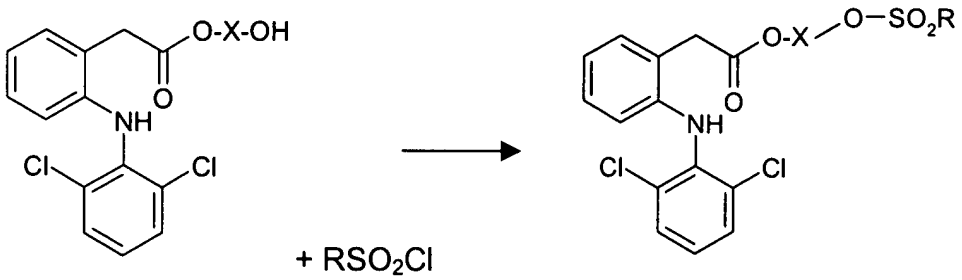
II[[,]]a; X = $-C_2H_4OC_2H_4-$

IIb; X = $-C_4H_8-$

IIc; X = $-C_2H_4OC_2H_4OC_2H_4-$

~~followed by,~~

~~step 2~~ (2), reacting the compounds of formula IIa, IIb or IIc with RSO_2Cl, wherein R is ~~as~~ defined ~~above~~ in claim 1, to obtain compounds of formula IIIa, IIIb or IIIc,



II

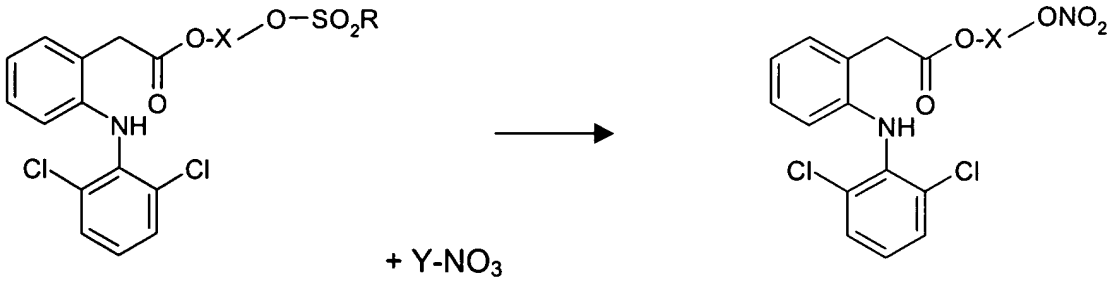
III[[,]]a; X = $-C_2H_4OC_2H_4-$

IIIb; X = $-C_4H_8-$

IIIc; X = $-C_2H_4OC_2H_4OC_2H_4-$

~~followed by,~~

~~step 3~~ (3), reacting the compounds of formula IIIa, IIIb or IIIc with a nitrate source $Y-NO_3$, wherein Y is ~~as~~ defined ~~above~~ in claim 1, to obtain compounds of formula IVa, IVb or IVc,



III

IV[[,]]a; X = $-C_2H_4OC_2H_4-$

IVb; X = $-C_4H_8-$

IVc; X = $-C_2H_4OC_2H_4OC_2H_4-$

~~followed by,~~

~~crystallising~~ crystallizing the compounds of formula IVa, IVb or IVc ~~using the following steps~~ by:

a) extracting the compound from the reaction solution into a solvent;

b) evaporating the solvent;

c) adding an anti-solvent and/or cooling

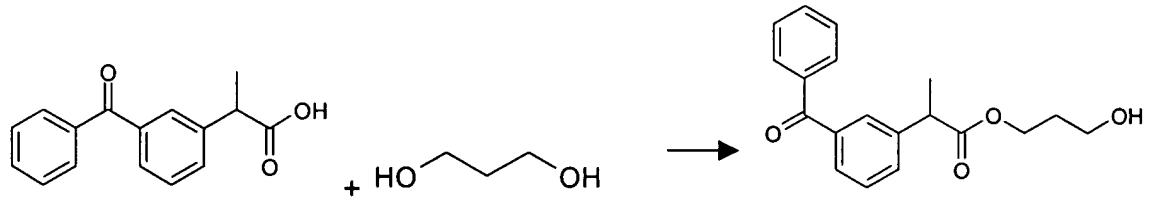
d) isolating the crystals formed, and optionally;

e) ~~recrystallising~~ recrystallizing the crystals formed ~~in step c);~~ or isolated ~~in step d)~~.

24. (Currently Amended) The process according to ~~any one of claims 1 to 23~~ claim 1, ~~whereby~~ wherein the chemical purity of Form A of compound IVa is above 95%.

25. (Currently Amended) A process for the ~~manufacturing~~ manufacture of NO donating ketoprofen of formula IVd comprising:

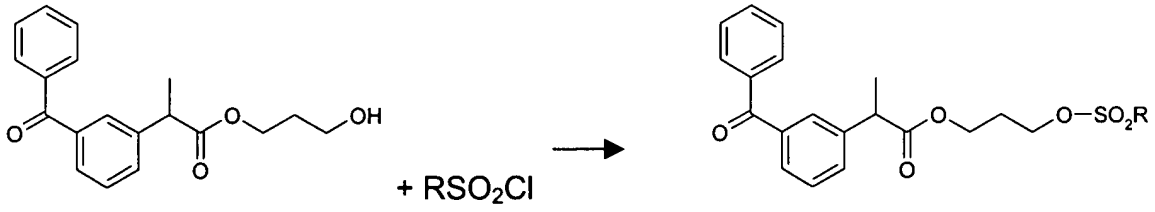
~~step 1~~ (1), reacting a compound of formula Id with 1,3-propanediol to obtain a compound of formula IId,



Id IId

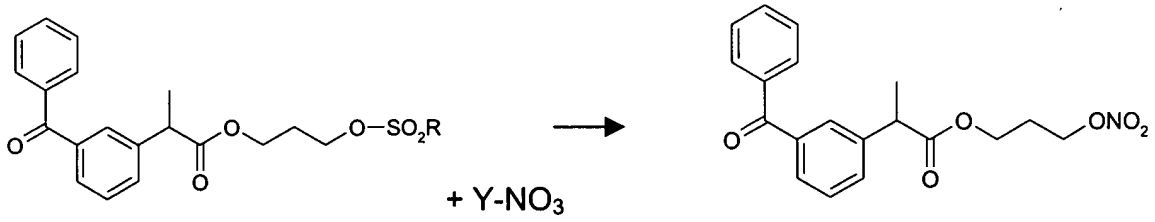
~~followed by,~~

~~step 2~~ (2), reacting the compound of formula IId with RSO_2Cl, wherein R is as defined in claim 1, to obtain a compound of formula IIId,



IId IIId

~~step 3~~ (3), reacting the compound of formula IIId with a nitrate source $Y\text{-}NO_3$, wherein Y is as defined in claim 1, to obtain a compound of formula IVd,



IIId IVd.

26. (Currently Amended) The process according to claim 25, ~~for the manufacturing of~~ wherein the compound of formula IVd is the *S*-enantiomer of NO donating ketoprofen ~~of formula IVd~~.

27. (Original) 2-[2-(nitrooxy)ethoxy]-ethyl {2-[(2,6-dichlorophenyl)amino]phenyl}acetate (IVa) in a substantially crystalline form.

28. (Currently Amended) The compound according to claim 27 in ~~anhydrate~~ anhydrous form.

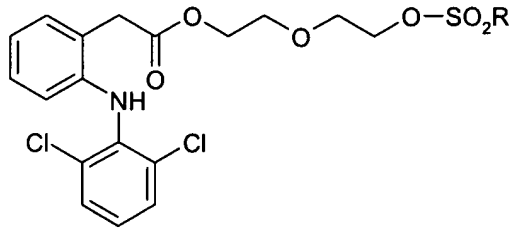
29. (Currently Amended) The compound according to claim 27, ~~characterised~~ characterized by the major peaks in the X-ray powder diffractogram shown ~~in the table~~ below:

D /Å	Relative		D/Å	Relative
12.7	M		3.52	M
8.7	W		3.49	M
8.1	W		3.44	W
6.3	S		3.41	VS
5.94	M		3.31	W
5.91	M		3.28	M
5.58	M		3.17	S
5.34	M		3.15	S
5.05	W		3.13	W
4.50	S		3.06	M
4.48	S		3.04	W
4.38	M		2.97	M
4.35	M		2.96	M
4.28	M		2.81	W
4.23	S		2.70	M
4.08	S		2.68	M
4.06	S		2.64	M
3.96	S		2.60	W
3.78	S		2.54	W
3.76	S		2.43	W
3.55	W			

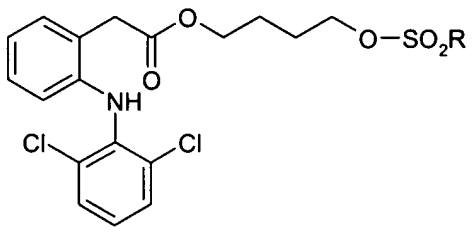
30. (Currently Amended) The compound according to claim 27, ~~characterised~~ characterized by having a monoclinic unit cell with parameters a = 13.79 Å, b = 11.90 Å, c = 13.01 Å, α = 90°, β = 94.0°, γ = 90°.

31. (Currently Amended) A process for the production of Form A of compound IVa ~~which comprises crystallising~~ comprising crystallizing 2-[2-(nitrooxy)ethoxy]ethyl {2-[(2,6-dichlorophenyl)amino]phenyl}acetate.

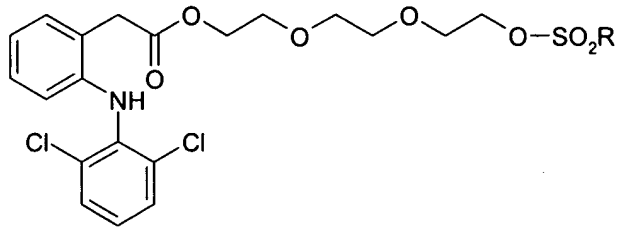
32. (Currently Amended) Compounds of formula IIIa, IIIb, IIIc and IIId:



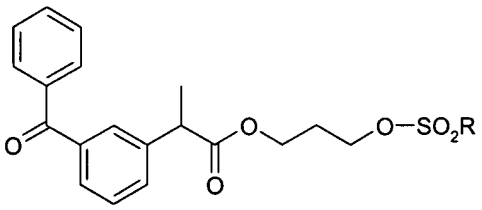
IIIa



IIIb



IIIc



IIId

wherein R is selected from the group consisting of C_1-C_8 alkyl, phenyl, phenylmethyl, C_1-C_4 alkylphenyl, halophenyl, nitrophenyl, acetylaminophenyl, halogen, CF_3, and *n*-C_4F_9.

33. (Currently Amended) Use of the process according to ~~any one of claims 1 to 21~~ claim 1 for the large scale manufacturing of the compounds of formula IVa, IVb, IVc and IVd.

34. (Original) Use of the compounds of formula III, $ML_{T1}A_{T2}$-X-O-SO_2R, wherein M, L, A, T1, T2, X and R are as defined in claim 1, as an intermediate for the manufacturing of a pharmaceutically active compound.

35. (Original) Use of intermediate compounds of formula IIIa, IIIb, IIIc and IIId as defined in claim 32, prepared according to the process described under step **1** and **2** of claim 1, for the manufacturing of a medicament for the treatment of pain and/or inflammation.

36. (Original) Use of Form A of compound IVa for the manufacturing of a medicament.

37. (Original) Use of Form A of compound IVa for the manufacturing of a medicament for the treatment of pain and/or inflammation.

38. (Original) A pharmaceutical formulation comprising a therapeutically effective amount of Form A of compound IVa, optionally in association with diluents, excipients or carriers.